

## SUNLIGHT AND NON-HODGKIN'S LYMPHOMA: A POPULATION-BASED COHORT STUDY IN SWEDEN

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Indirect evidence, notably ecological comparisons and an association with skin cancer, links non-Hodgkin's lymphoma (NHL) with exposure to sunlight. We conducted a population-based, nationwide cohort study with exposure to outdoor work inferred from job titles reported in the population and housing censuses in 1960 and/or 1970 and by classifying each individual's work and home addresses according to latitude. Follow-up for cancer incidence was accomplished through record linkages with the virtually complete Swedish Cancer Registry. The cohort included all Swedish residents who were recorded as gainfully employed in both censuses. Altogether 4,171,175 individuals contributing 69,639,237 person-years accrued through 1989 were included in the analyses. We identified 10,381 cases of NHL, 4,018 cases of chronic lymphocytic leukemia (CLL), 11,398 cases of malignant melanoma (MM) and 11,913 cases of squamous cell skin cancer (SCC). We calculated age-adjusted relative risks for NHL, CLL, MM and SCC in strata based on estimated residential and occupational sunlight exposure. Interaction effects were considered for pesticide and solvent exposure. NHL, MM and SCC, but not CLL, were positively associated with increasingly southerly residential latitude, with stronger associations seen for skin cancer compared to NHL. Occupational sun exposure was not associated with the risk of developing any of the studied cancers. Pesticides and solvents also were not related to an increased risk of NHL, nor did these exposures enhance effects of residential or occupational sunlight exposure. Our results provide some support for an association of sunlight exposure with NHL incidence based on the associations seen using geographic latitude of residence as a proxy for exposure. Although type of occupation may be an imperfect index of the biologically relevant ultraviolet (UV) light dose, our data on individual exposure are not consistent with an important role of sunlight in the etiology of NHL. *Int. J. Cancer* 80:641–645, 1999.

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The incidence of non-Hodgkin's lymphoma (NHL) is rising rapidly (3–4% per year on the average) in most Western countries (Hartge *et al.*, 1994; Swedish Cancer Registry, 1997). Only a fraction of the observed increase can be attributed to changing diagnostic practices (Hartge and Devesa, 1992), and the proportion of cases attributable to established or suspected risk factors is small.

It is well known that major changes in immune function are associated with a markedly increased risk of NHL (Levine and Hoover, 1992). There is suggestive evidence that exposure to ultraviolet (UV) light, an established cause of immune suppression (Kripke, 1994), may increase the risk of NHL (Zheng *et al.*, 1992; Cartwright *et al.*, 1994; Melbye *et al.*, 1996). Consistent with this hypothesis is a moderate ecological correlation between ambient levels of UV light and the incidence of NHL (Bentham, 1996; McMichael and Giles, 1996), and the finding that British migrants to Australia exhibit an upward shift in the risk of both NHL and malignant melanoma (MM) (McMichael and Giles, 1996). Further support comes from studies demonstrating a positive association between skin cancer, a surrogate indicator of UV light exposure, and NHL (Adami *et al.*, 1995; Frisch and Melbye, 1995; Hall *et al.*, 1995; Levi *et al.*, 1996). In the studies where chronic lymphocytic leukemia (CLL), considered to be a subgroup of NHL (Harris *et al.*,

1994), was included (Adami *et al.*, 1995; Levi *et al.*, 1996) similar risk associations were found. Therefore, CLL was included in the present study. However, other studies did not find support for a positive association between UV light exposure and risk of NHL (Hartge *et al.*, 1996; Freedman *et al.*, 1997).

To further assess the role of UV light in the risk of developing NHL we conducted a population-based, nationwide cohort study in Sweden using information from the Swedish Cancer-Environment Registry (CER) III, which links census data on place of residence and occupation in 1960 and 1970 with the virtually complete Swedish Cancer Registry (National Board of Health and Welfare, 1994). The findings for NHL were compared with the findings for MM and squamous cell skin cancer (SCC), the latter 2 malignancies regarded as causally linked to sunlight exposure (IARC, 1992). We also assessed the role of pesticides and solvents, since these exposures could potentially act as confounding factors, having been proposed as risk factors for NHL in previous occupational studies (Dich *et al.*, 1997; Savitz and Andrews, 1997).

### MATERIAL AND METHODS

#### Registry sources

**Population and Housing Censuses of 1960 and 1970.** In the National Population and Housing Censuses of 1960 and 1970, Statistics Sweden gathered information, through questionnaires to every household, about the entire Swedish population. The information included place of birth, home and work addresses, employment status, job title and industry for each household member (National Board of Health and Welfare, 1994). All Swedish residents are required by law to answer the census questionnaires and the completeness was estimated to exceed 99% (National Board of Health and Welfare, 1994). The industrial and occupational classifications used in the censuses are revised versions of the standards from the International Labor Office and the United Nations (International Labour Office, 1958; United Nations Statistical Office, 1958). A reliability study using a random sample from the 1960 census revealed a close agreement (95%) between the census data and the "true" occupation and industry codes (Brivkalne, 1964).

**Swedish Cancer and Cause of Death Registries.** The Swedish Cancer Registry, established in 1958, receives reports of all newly diagnosed malignant tumors. Notification is mandatory by law, with virtually all cases reported by the physician making the diagnosis and by the pathologist or cytologist confirming it. Almost 99% of all patients with diagnosed cancers are reported to the registry and 97% of the tumors are verified histologically (Swedish

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Cancer Registry, 1997). The virtually complete and continuously updated Cause of Death Registry provides information on all deceased individuals, including underlying and contributing causes of death (based on death certificates), date of death and age at death.

*Cancer-Environment Registry (CER).* The CER III merges incidence data from the Swedish Cancer Registry for the period 1971–1989 with demographic and occupational information from the 1960 and 1970 censuses (National Board of Health and Welfare, 1994), using the individually unique 10-digit national registration number assigned to each Swedish resident as identifier. To be included in the CER III, an individual had to be registered in both the 1960 and 1970 censuses and to be included in the cancer registry 1971–1989.

#### *Identification of the cohort*

The total cohort was defined as all Swedish residents who, according to the censuses, were recorded as gainfully employed in either 1960 or 1970, or both years. The date of entry into the cohort was set at 1 January 1971. Altogether 4,171,175 individuals contributing 69,639,237 person-years accrued through 1989 were included in the analyses. Males constituted 60% of the cohort; mean age at entry into the cohort was 46.8 years; 24% of the cohort members were less than 30 years old at entry, 56% were in the age group 30–59 years and 20% were more than 60 years old.

#### *Follow-up*

Follow-up was accomplished through record linkage between the cohort, identified through the censuses, and the Swedish Cancer Registry. Dates and causes of death among deceased were obtained from the Death Registry. Each cohort member contributed person-years from 1 January 1971 until a diagnosis of cancer, death or end of follow-up (31 December 1989), whichever occurred first. The mean follow-up time was 16.8 years.

#### *Exposure information from census data*

The country of Sweden was divided into 4 geographical regions based on latitude as follows: upper north (63–69°), lower north (60–62°), upper south (57–59°) and lower south (55–56°). Potential sunlight exposure was assessed by classifying each individual's work and home addresses according to latitude.

Each gainfully employed individual's occupation/industry combination in 1960 and 1970, respectively, was classified by an industrial hygienist into 3 categories (= type of occupation): primarily indoor work, work that combined indoor and outdoor exposure (mixed), and primarily outdoor work. Moreover, each subject's occupation and industry were classified with respect to probability (3 levels) and intensity (3 levels) of pesticide and solvent exposure: high, medium and low. In addition, we assessed the numbers of work-hours per week as categorized in the 1970 census according to 3 levels (<20, 20–34, 35+ hr).

Individuals were classified according to residence in any of the 3 largest cities in Sweden (Stockholm, Göteborg and Malmö). Also, we created an index of socioeconomic status with 5 levels based on job titles as described in detail elsewhere (Statistics Sweden, 1995).

#### *Statistical analyses*

First, the numbers of cases and person-years for each sex were summarized within 5-year age intervals for each category of the exposure variables studied. These data were then used to obtain age-adjusted relative risks (RR) in multivariate Poisson regression models using internal rates with age and the relevant exposure variable as independent variables. Risk was estimated by using the maximum likelihood method (Preston *et al.*, 1995). The effects of age, latitude, residence in a large city or not, type of occupation 1960 and 1970, socioeconomic status, number of work-hours per week and exposure to pesticides/solvents were analyzed and adjusted for in expanded multivariate models. Interaction effects were considered between the following variables: residential latitude and type of occupation; type of occupation and number of

work-hours per week; pesticides/solvents and residential latitude; pesticides/solvents and number of work-hours; pesticides/solvents and type of occupation.

The standardized incidence ratio (SIR), the ratio of the observed to the expected number of incident cancers, was also used to estimate the risk of NHL, CLL, MM and SCC for the different exposure categories. The expected number of cancers was calculated by multiplying the observed number of person-years in the cohort by age-, sex- and calendar-year-specific cancer incidence rates derived from the entire Swedish population. We excluded cancers detected incidentally at autopsy, both in the cohort and in the expected rates. The SIRs (based on external comparisons) were similar to the RRs from Poisson regression, indicating that the studied cohort was representative of the general population (data not shown).

## RESULTS

Overall, we identified 10,381 cases of NHL (ICD-7 codes 200 and 202), 4,018 cases of CLL (ICD-7 code 204.1), 11,398 cases of MM (ICD-7 code 190) and 11,913 cases of SCC (ICD-7 code 191). We present the results from analyses based on the 1960 census data because there were no major differences compared to the results based on 1970 or the combined 1960 and 1970 censuses. Since multivariate modeling with available exposure variables (type of occupation and latitude) and covariates (solvents, pesticides, socioeconomic status, work-hours per week and large city) did not substantially change the studied RR estimates, in the following we present the RRs adjusted only for age.

Table I gives the sex-specific age-adjusted relative risks of NHL, CLL, MM and SCC related to geographic latitude of residence in 1960 and type of occupation. The vast majority of the subjects lived and worked within the same latitude category in both 1960 and 1970. In both sexes, and in all diagnostic groups except for CLL, the RRs were increased for those residing in more southerly latitudes compared with those living in the upper north. The risk estimates in the south relative to the north were higher for MM and SCC than for NHL and increased significantly with a more southern location of the home/workplace (NHL: *p*-value for trend = 0.0005 vs. 0.013 for men and women, respectively). Individuals with primarily outdoor work or a combination of outdoor and indoor work did not have an excess risk of any of the studied malignancies compared to individuals with their work mainly indoors except for SCC among women. We also explored the possible interaction between indoor/outdoor occupation and the number of work-hours per week (<20, 20–34, 35+ hr), but found no significant interaction (data not shown).

Table II shows analyses of effects of latitude stratified by occupational type and sex. The highest risks were seen among subjects with mixed indoor/outdoor occupations in the most southern part of Sweden. Although there was a tendency toward a steeper north-south gradient among men and women with a combined indoor/outdoor type of work, there was no clear dose-dependent effect modification by extent of outdoor activities at work.

Age-adjusted analyses of occupational pesticide and solvent exposure and the risk of NHL did not reveal any association with NHL (data not shown). Table III shows age-adjusted RRs of NHL by latitude and type of occupation among individuals classified as most exposed to pesticides and/or solvents. The results were not enhanced by exposure to pesticides and solvents.

## DISCUSSION

Our results provide limited support for a modest association of potential sunlight exposure with NHL, but not with CLL incidence using geographic latitude of residence as a surrogate variable for exposure. However, the association of sunlight exposure with the risk for NHL, CLL or skin cancer is not supported by our

**TABLE I** – AGE-ADJUSTED RRs (95% CONFIDENCE INTERVALS) OF NHL, CLL, MM AND SCC AMONG MEN AND WOMEN, RELATED TO LATITUDE AND TYPE OF OCCUPATION<sup>1</sup>

|             | NHL                       |                           | CLL                       |                         | MM                        |                           | SCC                       |                         |
|-------------|---------------------------|---------------------------|---------------------------|-------------------------|---------------------------|---------------------------|---------------------------|-------------------------|
|             | Men                       | Women                     | Men                       | Women                   | Men                       | Women                     | Men                       | Women                   |
| Latitude    |                           |                           |                           |                         |                           |                           |                           |                         |
| Upper north | 1.00 (480)<br>ref.        | 1.00 (236)<br>ref.        | 1.00 (351)<br>ref.        | 1.00 (78)<br>ref.       | 1.00 (347)<br>ref.        | 1.00 (234)<br>ref.        | 1.00 (634)<br>ref.        | 1.00 (133)<br>ref.      |
| Lower north | 1.10 (2,025)<br>1.00–1.22 | 1.22 (1,393)<br>1.06–1.40 | 0.98 (1,207)<br>0.87–1.10 | 0.93 (370)<br>0.73–1.19 | 2.06 (2,522)<br>1.84–2.30 | 1.52 (1,610)<br>1.33–1.75 | 1.40 (3,121)<br>1.29–1.53 | 1.36 (935)<br>1.13–1.63 |
| Upper south | 1.09 (1,739)<br>0.98–1.21 | 1.17 (973)<br>1.01–1.35   | 0.99 (1,081)<br>0.88–1.12 | 0.98 (280)<br>0.76–1.26 | 2.38 (2,486)<br>2.13–2.66 | 2.00 (1,604)<br>1.74–2.29 | 1.81 (3,634)<br>1.66–1.97 | 1.83 (904)<br>1.52–2.19 |
| Lower south | 1.21 (762)<br>1.08–1.35   | 1.26 (482)<br>1.08–1.40   | 0.98 (417)<br>0.84–1.13   | 0.81 (107)<br>0.60–1.08 | 2.40 (999)<br>2.12–2.71   | 2.24 (806)<br>1.94–2.59   | 2.10 (1,644)<br>1.92–2.30 | 2.21 (512)<br>1.82–2.64 |
| Occupation  |                           |                           |                           |                         |                           |                           |                           |                         |
| Indoor      | 1.00 (4,136)<br>ref.      | 1.00 (1,912)<br>ref.      | 1.00 (1,759)<br>ref.      | 1.00 (584)<br>ref.      | 1.00 (4,111)<br>ref.      | 1.00 (2,511)<br>ref.      | 1.00 (5,256)<br>ref.      | 1.00 (1,702)<br>ref.    |
| Mixed       | 1.02 (1,020)<br>0.95–1.09 | 1.12 (49)<br>0.84–1.49    | 1.08 (465)<br>0.98–1.20   | 0.96 (13)<br>0.55–1.66  | 0.84 (828)<br>0.78–0.90   | 1.07 (57)<br>0.82–1.39    | 0.97 (1,259)<br>0.91–1.03 | 1.13 (44)<br>0.84–1.53  |
| Outdoor     | 0.93 (1,739)<br>0.88–0.98 | 0.83 (73)<br>0.66–1.05    | 1.03 (877)<br>0.95–1.12   | 0.86 (25)<br>0.58–1.28  | 0.70 (1,185)<br>0.65–0.74 | 0.89 (85)<br>0.72–1.10    | 0.96 (2,668)<br>0.91–1.00 | 1.31 (118)<br>1.09–1.58 |

<sup>1</sup>Number of cases in parentheses. ref., reference case.**TABLE II** – AGE-ADJUSTED RRs AND 95% CONFIDENCE INTERVALS OF NHL AMONG MEN AND WOMEN, RELATED TO LATITUDE AND TYPE OF OCCUPATION IN 1960

| Latitude    | Type of occupation |                   |                   |                   |                   |                   |
|-------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
|             | Indoor             |                   | Mixed             |                   | Outdoor           |                   |
|             | Men                | Women             | Men               | Women             | Men               | Women             |
| Upper north | 1.00<br>ref.       | 1.00<br>ref.      | 1.00<br>ref.      | 1.00<br>ref.      | 1.00<br>ref.      | 1.00<br>ref.      |
| Lower north | 1.06<br>0.94–1.19  | 1.27<br>1.05–1.55 | 1.04<br>0.84–1.29 | 1.26<br>0.48–3.35 | 1.06<br>0.91–1.23 | 1.24<br>0.54–2.83 |
| Upper south | 1.04<br>0.92–1.17  | 1.21<br>0.99–1.48 | 1.04<br>0.84–1.30 | 1.14<br>0.39–3.33 | 1.07<br>0.93–1.24 | 0.83<br>0.36–1.93 |
| Lower south | 1.15<br>1.00–1.31  | 1.32<br>1.06–1.64 | 1.40<br>1.10–1.78 | 1.99<br>0.70–5.64 | 1.14<br>0.95–1.35 | 1.43<br>0.65–3.14 |

**TABLE III** – AGE-ADJUSTED RRs AND 95% CONFIDENCE INTERVALS (CI) OF NHL AMONG MEN AND WOMEN WITH HIGH OCCUPATIONAL PESTICIDE OR SOLVENT EXPOSURE, BY LATITUDE AND TYPE OF OCCUPATION

|             | Men             |      |           | Women           |      |           |
|-------------|-----------------|------|-----------|-----------------|------|-----------|
|             | Number of cases | RR   | 95% CI    | Number of cases | RR   | 95% CI    |
| Latitude    |                 |      |           |                 |      |           |
| Upper north | 272             | 1.00 | ref.      | 39              | 1.00 | ref.      |
| Lower north | 701             | 1.08 | 0.94–1.25 | 109             | 1.01 | 0.70–1.46 |
| Upper south | 874             | 1.08 | 0.94–1.24 | 130             | 0.91 | 0.64–1.31 |
| Lower south | 405             | 1.27 | 1.08–1.48 | 79              | 1.00 | 0.68–1.47 |
| Occupation  |                 |      |           |                 |      |           |
| Indoor      | 774             | 1.00 | ref.      | 143             | 1.00 | ref.      |
| Mixed       | 241             | 1.05 | 0.90–1.21 | 16              | 1.38 | 0.82–2.31 |
| Outdoor     | 1,261           | 0.98 | 0.89–1.07 | 70              | 0.87 | 0.65–1.17 |

occupational data, where job title and industry served as proxy exposure information.

Some previous studies on NHL and sunlight have used data with exposure estimated by place of residence alone (McMichael and Giles, 1996; Bentham, 1996). Other studies have used skin cancer incidence as a proxy variable for UV light exposure (Adami *et al.*, 1995; Frisch and Melbye, 1995; Hall *et al.*, 1995; Levi *et al.*, 1996). In contrast with the U.S. mortality case-control study by Freedman *et al.* (1997), our study revealed increases in risk for NHL, MM and SCC among persons residing at more southerly latitudes. One explanation for the discrepancy between the results could be differences in the study populations since “white” persons in England and Scandinavia have lighter skin compared to the more diverse “white” U.S. population. Therefore, the greater possibility of misclassification in the U.S. study might make it harder to detect low level risks since the population includes persons with darker

skin. We have no explanation regarding why NHL but not CLL showed a positive association with more southerly latitudes; in previous studies using skin cancer incidence as a proxy variable for sunlight exposure, similar risk associations were seen (Adami *et al.*, 1995; Levi *et al.*, 1996).

Immunologic dysfunctions have been shown to increase the risk of NHL (Levine and Hoover, 1992). The biological plausibility for an association between UV light and NHL is reasonable since UV light has a well-established systemic immune suppressive effect (Cridland and Saunders, 1994; Kripke, 1994). Moreover, it has been shown that mice have an increased incidence of lymphomas after UV light exposure (Ebbesen, 1981). In humans, UV irradiation temporarily attenuates or chronically affects hypersensitivity reactions toward antigens (Hersey *et al.*, 1983a,b; Vermeer *et al.*, 1991; Cooper *et al.*, 1992).

Previous investigations of occupation and risk of NHL have focused mainly on occupations involving exposure to pesticides and solvents. Pesticides include a wide number of chemical compounds (Dich *et al.*, 1997) and are used predominantly in agriculture, horticulture and vector control as well as in forestry and livestock production (IARC, 1994). Benzene, a solvent recently associated with NHL (Savitz and Andrews, 1997), is used primarily during the processing of petroleum products, in the coking of coal, in the rubber industry, in consumer products and as a component of gasoline. Even though some populations exposed to certain pesticides and solvents have been reported to have an excess risk of NHL, the evidence is not conclusive (Dich *et al.*, 1997; Savitz and Andrews, 1997), and we found no support for such associations in our study.

Our study had the advantage of using individual data on occupation, industry, work-hours, geographic latitude of residence and workplace, residence in large cities vs. elsewhere, classification



of socioeconomic status, estimated occupational exposures to pesticides and solvents, and of using cancer incidence as the outcome measure. The potential misclassification of exposures that are inferred from job titles and industry categories in follow-up studies is non-differential but often substantial, which most often (Dosemeci *et al.*, 1990) reduces and obscures associations. Also, elevated risks in individuals with a rare exposure will be missed if those persons are grouped with non-exposed persons. To reduce this problem, we evaluated risk factors by developing job-exposure matrices (JEM) using information on both occupation and industry (Hoar *et al.*, 1980). Since the probability of exposure and the intensity of exposure differ between different types of occupations and industries, we assigned 3 levels of probability and intensity to industries and occupations deemed to have the exposures of interest. This may have a notable effect in reducing exposure misclassification when using a JEM (Dosemeci *et al.*, 1994).

However, even with careful assessment by an experienced industrial hygienist in developing job/industry exposure matrices, we acknowledge that there may still be important misclassification in estimating an individual cohort member's exposure to sunlight. This is to some extent explained by great variations in actual work content within single job titles or industry categories and to practices of using or not using hats and protective clothing during work-hours, but also may be further aggravated by differential patterns of leisure-time sunlight exposure (including the use of sunbeds) among occupational categories. For instance, indoor workers may be more inclined to excessive and unprotected sunbathing habits than are those who are exposed to the sun on a daily basis year-round. It is unknown if certain patterns of exposure

to sun are more associated than others with immunosuppression or NHL, and if the gradual skin adaptation in the chronically exposed is of importance. Further, the exposure classification was based on data collection at 2 points in time (1960 and 1970), not lifetime history. Whether NHL, like MM, is associated with acute exposure during childhood and adolescence remains unknown and could not be elucidated by our data. The failure of our indoor-outdoor JEM to demonstrate any clear effects on the risk of MM or SCC implies that the classification, for whatever reason, was unable to capture the biologically relevant aspects of UV light exposure. This finding is in accordance with other studies using similar surrogate measures (Pukkala and Saarni, 1996; Freedman *et al.*, 1997) where no major differences in cancer risk comparing indoor and outdoor workers were revealed. Since the detrimental impact of UV radiation is influenced by factors such as solar height, ozone, ground reflectance, clouds and altitude (Josefsson, 1986), latitude seems to be a more accurate measure when evaluating health effects of exposure to sun (Josefsson, 1986). Moreover, place of residence is unlikely to have been severely misclassified. To resolve the apparent inconsistency between associations observed in analyses based on residence, with little misclassification, and those based on a JEM with the potential for considerable misclassification of sunlight exposure, it appears reasonable to assign more weight to the former.

In conclusion, although our residential latitude data provide some, albeit weak and indirect, support for a role of UV light exposure in the etiology of NHL in Sweden, our findings based on individual occupational data are not consistent with this hypothesis. The issue thus warrants further studies.

#### REFERENCES

- ADAMI, J., FRISCH, M., GLIMELIUS, B., YUEN, J. and MELBYE, M., Evidence of an association between non-Hodgkin's lymphoma and skin cancer. *Brit. med. J.*, **310**, 1491–1495 (1995).
- BENTHAM, G., Association between incidence of non-Hodgkin's lymphoma and solar ultraviolet radiation in England and Wales. *Brit. med. J.*, **312**, 1128–1131 (1996).
- BRIVKALNE, M., *The control study made in connection with the 1960 census of population. Statistical reports B*, Statistics Sweden, Stockholm (1964).
- CARTWRIGHT, R., McNALLY, R. and STAINES, A., The increasing incidence of non-Hodgkin's lymphoma (NHL): the possible role of sunlight. *Leukemia Lymphoma*, **14**, 387–394 (1994).
- COOPER, K.D., OBERHELMAN, L., HAMILTON, T.A., BAADSGAARD, O., TERHUNE, M., LEVEE, G., ANDERSON, T. and KOREN, H., UV exposure reduces immunization rates and promotes tolerance to epicutaneous antigens in humans: relationship to dose, CD1a<sup>+</sup>DR<sup>+</sup> epidermal macrophage induction, and Langerhans cell depletion. *Proc. nat. Acad. Sci. (Wash.)*, **89**, 8497–8501 (1992).
- CRIDLAND, N.A. and SAUNDERS, R.D., *Cellular and molecular effects of UVA and UVB*, Her Majesty's Stationery Office, London (1994).
- DICH, J., ZAHM, S.H., HANBERG, A. and ADAMI, H.-O., Pesticides and cancer. *Cancer Causes Control*, **8**, 420–443 (1997).
- DOSEMECI, M., COCCO, P., GÓMEZ, M., STEWART, P. and HEINEMAN, E.F., Effects of three features of a job-exposure matrix on risk estimates. *Epidemiology*, **5**, 124–127 (1994).
- DOSEMECI, M., WACHOLDER, S. and LUBIN, J., Does non-differential misclassification of exposure always bias a true effect towards the null value? *Amer. J. Epidemiol.*, **127**, 746–748 (1990).
- EBBESSEN, P., Enhanced lymphoma incidence in BALB/c mice after ultraviolet light treatment. *J. nat. Cancer Inst.*, **67**, 1077–1078 (1981).
- FREEDMAN, D.M., ZAHM, S.H., HOAR, S. and DOSEMECI, M., Residential and occupational exposure to sunlight and mortality from non-Hodgkin's lymphoma: composite (threefold) case-control study. *Brit. med. J.*, **314**, 1451–1455 (1997).
- FRISCH, M. and MELBYE, M., New primary cancers after squamous cell skin cancer. *Amer. J. Epidemiol.*, **141**, 916–922 (1995).
- HALL, P., ROSENDAHL, I., MATTSOON, A. and EINHORN, S., Non-Hodgkin's lymphoma and skin malignancies—shared etiology? *Int. J. Cancer*, **62**, 519–522 (1995).
- HARRIS, N.L. and 18 OTHERS, A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood*, **84**, 1361–1392 (1994).
- HARTGE, P. and DEVESA, S.S., Quantification of the impact of known risk factors on time trends in non-Hodgkin's lymphoma incidence. *Cancer Res.*, **52** (Suppl.), 5566–5569 (1992).
- HARTGE, P., DEVESA, S.S. and FRAUMENI, J.F., JR., Hodgkin's and non-Hodgkin's lymphoma. In R. Doll, J.F. Fraumeni, Jr. and C.S. Muir (eds.), *Cancer surveys: trends in cancer incidence and mortality*, Vol. **19/20**, pp. 423–453, Cold Spring Harbor Laboratory Press, Plainview, NY (1994).
- HARTGE, P., DEVESA, S.S., GRAUMAN, D., FEARS, T.R. and FRAUMENI, J.F., JR., Non-Hodgkin's lymphoma and sunlight. *J. nat. Cancer Inst.*, **88**, 298–300 (1996).
- HERSEY, P., HARAN, G., HASIC, E. and EDWARDS, A., Alteration of T cell subsets and induction of suppressor T cell activity in normal subjects after exposure to sunlight. *J. Immunol.*, **31**, 171–174 (1983a).
- HERSEY, P., HASIC, E., EDWARDS, A., BRADLEY, M., HARAN, G. and MCCARTHY, W.H., Immunological effects of solarium exposure. *Lancet*, **1**, 545–548 (1983b).
- HOAR, S.K., MORRISON, A.S., COLE, P. and SILVERMAN, D.T., An occupation and exposure linkage system for the study of occupational carcinogenesis. *J. Occup. Med.*, **22**, 722–726 (1980).
- INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC), *Monographs on the evaluation of carcinogens to humans. Solar and ultraviolet radiation*, Vol. **55**, pp. 73–138, IARC, Lyon (1992).
- INTERNATIONAL LABOUR OFFICE, *International standard classification of occupations*, International Labour Office, Geneva (1958).
- JOSEFSSON, W., Solar ultraviolet radiation in Sweden. SMHI report **53. Meteorology and Climatology** SMHI, Norrhöping, Sweden (1986).
- KRIPKE, M.L., Ultraviolet radiation and immunology: something new under the sun. *Cancer Res.*, **14**, 387–394 (1994).
- LEVI, F., RANDIMBISON, L., TE, V.-C. and LA VECCHIA, C., Non-Hodgkin's lymphomas, chronic lymphocytic leukaemias and skin cancers. *Brit. J. Cancer*, **74**, 1847–1850 (1996).
- LEVINE, P.H. and HOOVER, R.N., The emerging epidemic of non-Hodgkin's lymphoma: current knowledge regarding etiological factors. *Cancer*, **52** (Suppl.), 5425–5574 (1992).
- McMICHAEL, A.J. and GILES, G.G., Have increases in solar ultraviolet exposure contributed to the rise in incidence of non-Hodgkin's lymphoma? *Brit. J. Cancer*, **73**, 945–950 (1996).

- MELBYE, M., ADAMI, H.-O., HJALGRIM, H. and GLIMELIUS, B., Ultraviolet light and non-Hodgkin's lymphoma. *Acta Oncol.*, **35**, 655–657 (1996).
- NATIONAL BOARD OF HEALTH AND WELFARE, *The Swedish Cancer Environment Registry 1960–70*, National Board of Health and Welfare, Stockholm (1994).
- PRESTON, D.L., LUBIN, J.H. and PIERCE, D.A., *EPICURE: generalized regression models for epidemiologic data*, HiroSoft, Seattle (1995).
- PUKKALA, E. and SAARNI, H., Cancer incidence among Finnish seafarers, 1967–92. *Cancer Causes Control*, **7**, 231–239 (1996).
- SAVITZ, D.A. and ANDREWS, K.W., Review of epidemiologic evidence on benzene and lymphatic and hematopoietic cancers. *Amer. J. industr. Med.*, **31**, 287–295 (1997).
- SWEDISH CANCER REGISTRY, *Cancer incidence in Sweden 1994*, National Board of Health and Welfare, Stockholm (1997).
- STATISTICS SWEDEN, Swedish socioeconomic classification. *Reports on statistical co-ordination 1982: 4*, Statistics Sweden, Stockholm (1995).
- UNITED NATIONS STATISTICAL OFFICE, *International standard industrial classification of all economic activities*, United Nations Statistical Office, New York (1958).
- VERMEER, M., SCHMIEDER, G.J., YOSHIKAWA, T., VAN DER BERG, J.W., METZMAN, M.S., TAYLOR, J.R. and STREILEIN, J.W., Effects of ultraviolet B light on cutaneous immune responses of humans with deeply pigmented skin. *J. invest. Dermatol.*, **97**, 729–734 (1991).
- ZHENG, T., MAYNE, S., BOYLE, P., HOLDFORD, T.R., LIU, W.L. and FLANNERY, J., Epidemiology of non-Hodgkin lymphoma in Connecticut 1935–1988. *Cancer*, **70**, 840–849 (1992).